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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/644,052

08/19/2003

Arthur M. Krieg

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EXAMINER

ARCHIE, NINA

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/644,052	Applicant(s) KRIEG ET AL.	
	Examiner Nina A. Archie	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 100-107 is/are pending in the application.
- 4a) Of the above claim(s) 1-99 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 100-107 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 3-11-09. Claims 100-107 are pending and under examination. Claim 100 has been amended. Claims 1-5, 12-17, 22-28, 32, 36, 39, 44, 46, 48-49, 66-67, 70, 88, and 94-99 are cancelled.

Sequence Requirements

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a) (1) and (a) (2). It is noted that claims 101 and 102 does not disclose a SEQ ID NO: in the claims. Applicant are required to an amend the claims disclosing the SEQ ID NO: with the sequences in 101 and 102. However, this application fails to comply with the requirements of 37 C.F.R. § 1.821-1.825 for the reason(s) set forth below. Full compliance with the sequence rules is required in response to this office action.

Objections/Rejections Withdrawn

3. In view of the Applicant's amendment and remark following objections/rejections are withdrawn.

- a) Rejection to claim 49 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Application No. 11/361,313 is withdrawn in light of applicant cancellation of claim.
- b) Rejection of claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 44, 49, 66-67, 97-98, and 100 under 35 U.S.C. 102(b) as being anticipated by Krieg et al WO/01/22972A2 is withdrawn from consideration due lack of stabilized and phosphodiester internucleotide linkages at specific positions.
- c) The rejection of claims 1-2, 12, 14, 16-17, 22, 24, 26-27, 44, 49, 66-67, 97-98 and 100 under 35 U.S.C. 103(a) as being unpatentable in view of Krieg et al WO/01/22972A2 April 5, 2001 is withdrawn.

Claim Rejection Maintained - 35 USC § 103

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 100-104 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As to claims 100 and 105 independent claims, recites the length 16-40 nucleotides although SEQ ID NO: 313 comprises 16-24 nucleotides. Therefore, the skilled artisan would not be readily apprised of the metes and bounds of the length of the oligonucleotide nor how to assess such. It is unclear how to interpret what the length of the structure of the oligonucleotide is.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 100-107 under 35 U.S.C. 103(a) as being unpatentable in view of Krieg et al WO/01/22972A2 April 5, 2001 and Samani et al Antisense and Nucleic Acid Drug Development 2001 Vol. 11 pgs. 129-136.

The claims are drawn to an oligonucleotide having the following structure: 5' T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3' (SEQ ID NO: 313), wherein * refers to the presence of a stabilized internucleotide linkage, wherein _ refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 16-40 nucleotides (claim 100), wherein the oligonucleotide consists of 5' T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3' (claim 101), wherein the oligonucleotide consist of 5' T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3' (claim 102), formulated in a composition, further comprising a carrier (claim 103), wherein the stabilized internucleotide linkage is a phosphorothioate internucleotide linkage (claim 104); an oligonucleotide having the following structure: 5'

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T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3', wherein * refers to the presence of a stabilized internucleotide linkage, and each _ refers a phosphodiester internucleotide linkage, and wherein the oligonucleotides is 24 nucleotides (claim 105), a pharmaceutical composition comprising an oligonucleotide as defined as an oligonucleotide having the following structure: 5'

T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3' (SEQ ID NO: 313), wherein * refers to the presence of a stabilized internucleotide linkage, wherein * refers to the presence of a stabilized internucleotide linkage, and wherein _ refers to the presence of a phosphodiester internucleotide linkage and wherein the oligonucleotide has a length of 16-40 nucleotides (claim 106); a pharmaceutical composition comprising an oligonucleotide as defined as an oligonucleotide having the following structure: 5'

T*C_G*T*C_G*T*T*T*T*G*A*C_G*T*T*T*T*G*T*C_G*T*T 3', wherein * refers to the presence of a stabilized internucleotide linkage, and each _ refers a phosphodiester internucleotide linkage, and wherein the oligonucleotides is 24 nucleotides.

Krieg et al WO01/22972A2 teach sequence 343 s wherein s=phosphorothioate linkages which correlates to SEQ ID NO: 313 wherein * refers to the presence of a stabilized internucleotide linkage and wherein the oligonucleotide has a length of 16-40 nucleotides (see table 4 sequence 343 pg. 45).

Krieg et al teaches an oligonucleotide comprising N₁-C_G-N₂-C_G-N₃ wherein N₁, N₂, and N₃ are each independently a nucleic acid sequence of 0-20 nucleotides in length and wherein _ indicates an internal phosphodiester internucleotide linkage (see pgs. 2-12, pgs. 18-24, pgs. 27-30, and pg. 34), wherein the immunostimulatory nucleic acid molecule is 4-100 nucleotides long (see pg. 8 lines 8-13). Krieg et al teach a chimeric combination of phosphodiester and phosphorothioate oligonucleotide because a cell may have a problem taking up a plasmid vector in the presence of completely phosphorothioate nucleic acid (see pgs. 36-37).

Krieg et al is relied upon as set forth supra. Although, Krieg et al is silent to teaching a phosphodiester internucleotide linkage between C and G in SEQ ID NO: 313 in an oligonucleotide, formulated in a composition, further comprising a carrier.

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Krieg et al teach immunostimulatory nucleotides having a phosphodiester internucleotide linkage are CG. Furthermore, Krieg et al teach nucleic acid that has a phosphodiester backbone linkage the nucleic acid will only have minimal if any effect on the biological activity of the nucleic acid.

Samani et al phosphodiester are rapidly degraded by serum intracellular nuclease (see Samani et al pg. 129). Krieg et al teach an oligonucleotide formulated in a composition further comprising a carrier (see pg. 7 lines 30-35, pg. 8 lines 1-15, and pg. 10 lines 1-25).

It would have been prima facie obvious at the time the invention was made to place a phosphodiester between the C and the G to produce a oligonucleotide with a CpG that has a phosphodiester internucleotide linkage and modify the oligonucleotide with stabilized internucleotide linkages such as phosphorothioate as taught by Krieg et al because Krieg et al teach a chimeric combination of phosphodiester and phosphorothioate oligonucleotide because a cell may have a problem taking up a plasmid vector in the presence of completely phosphorothioate nucleic acid.

One would have reasonable expectation of success because phosphodiester oligonucleotides with a minimum of phosphorothioate linkages is well known in the art as disclosed by (Samani et al. 2001 Antisense and Nucleic Acid Drug Development Vol. 11 pgs. 129-136).

Conclusion

6. No claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie

Examiner

GAU 1645

REM 3B31

/Robert A. Zeman/

for Nina Archie, Examiner of Art Unit 1645